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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 06/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,651	SCHOR ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9,29,60 and 61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,5 and 29* is/are allowed.

6)☒ Claim(s) *1, 7-9, 60 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed April 19, 2006, is acknowledged and has been entered. Claims 1, 4, 5, 7, 9, and 61 have been amended.

2. Claims 1, 4, 5, 7-9, 29, 60, and 61 are currently under prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

Drawings

5. Receipt of the replacement drawing filed April 19, 2006, is acknowledged. The drawing depicting Figure 2 is acceptable.

Allowable Subject Matter

6. Claims 4, 5, and 29 are allowable.

Priority

7. Applicant's claim under 35 USC § 120 for benefit of the earlier filing date of the PCT Application No. PCT/GB98/03766, filed December 15, 1998, which claims benefit of United Kingdom Patent Application No. 9726539.1, filed December 16, 1997, is acknowledged.

However, claims 1, 7-9, 60, and 61 do not properly benefit under 35 U.S.C. § 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure. In particular, it is noted that the subject matter of claims 1, 7-9, 60, and 61 is not adequately described in the prior applications, as neither

application teaches a genus of polynucleotides having at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which encode polypeptides comprising the amino acid sequence of SEQ ID NO: 41 and having the additional characteristics recited in claim 1, such as the characteristic of having at least 30% of the migration stimulation factor activity of a polypeptide having the amino acid sequence of SEQ ID NO: 2. More pointedly, although the specifications of the prior applications describe polynucleotides encoding a polypeptide comprising SEQ ID NO: 2, neither specification describes the far broader genus of polynucleotides encoding polypeptides comprising SEQ ID NO: 41. This issue is further addressed below in the new rejection of claims 1, 7-9, 60, and 61, as failing to satisfy the written description requirement.

To receive benefit of the earlier filing date under 35 USC § 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Accordingly, the effective filing date of the claims 1, 7-9, 60, and 61 is deemed the filing date of the instant application, namely October 10, 2000.

Grounds of Objection and Rejection Withdrawn

8. Unless specifically reiterated below, Applicant's amendment and/or arguments filed April 19, 2006, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed January 25, 2006.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

9. The rejection of claims 1, 7-9, 60, and 61 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At pages 7-9 of the amendment filed April 19, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued that the written description requirement has been met because the claims are directed to a genus of polynucleotides having at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, wherein said polynucleotides encode polypeptides comprising the amino acid sequence of SEQ ID NO: 41, have at least 30% of the migration stimulation factor activity (i.e., the ability to stimulate adult fibroblast migration into a collagen gel) of a polypeptide comprising SEQ ID NO: 2, and elicit antibodies that recognize the polypeptide of SEQ ID NO: 2 but not fibronectin. Moreover, Applicant has argued the claims are thus directed to a genus having "no substantial variation" (amendment, page 7, paragraph 3).

In response, as noted in the preceding Office action, the term "homology" is defined, for example, by Merriam-Webster Online Dictionary, which available on the Internet at http://www.merriam-webster.com/, as "similarity of nucleotide or amino-acid sequence in nucleic acids, peptides, or proteins" (copyright 2005 by Merriam-Webster, Incorporated). Homology or similarity of nucleic acid sequences may be evaluated by relatively subjective criterion, or it may be objectively measured using any of wide variety of differing criterion.

As such, the claims are directed to a genus of polynucleotides, which have polynucleotides sequences that do in fact vary substantially, provided they may be evaluated by any of a variety of relatively subjective, or perhaps more objective criteria to have some similarity to a polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and provided the polypeptides encoded thereby comprise the amino acid sequence of SEQ ID NO: 41.

SEQ ID NO: 41 is an amino acid sequence spanning the carboxy-terminal 10 amino acids of the disclosed polypeptide having the amino acid sequence set forth as SEQ ID NO: 2; the specification however attributes or associates no specific activity of the polypeptide of SEQ ID NO: 2, or indeed that of any of the genus of polypeptides to which the claims refer, to this particular amino acid sequence.

Thus, although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, which elicit antibodies that recognize a polypeptide comprising SEQ ID NO: 2 but not fibronectin, these polypeptides are not described with the requisite degree of particularity to permit the skilled artisan to immediately envision, recognize or distinguish at least a substantial number of the polypeptides, or the nucleic acid molecule encoding the polypeptides. Moreover, the polypeptides encoded by the members of the claimed genus of nucleic acid molecules have not been described as having a particularly identifying (i.e., substantial) structural feature shared by at least most of the polypeptides encoded by the claimed nucleic acid molecules, which correlates with their common ability to stimulate adult skin fibroblasts migration into collagen gel to the requisite extent or to elicit antibodies that bind the polypeptide of SEQ ID NO: 2 but not fibronectin.

Again, the specification describes only one polypeptide encoded by the claimed genus of nucleic acid molecules, namely the polypeptide of SEQ ID NO: 2. Neither the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 (e.g., the nucleic acid molecule of SEQ ID NO: 3) nor the polypeptide itself are not described in sufficient and detailed manner, so as to reasonably be considered representative of the genus, as a whole, since there is no disclosure of the presence of a shared, particularly identifying structural feature, which in this case is necessarily a common antigenic determinant (i.e., the epitope to which an antibody that recognizes the protein encoded by the claimed nucleic acid molecule, which is not presented by fibronectin), that correlates with their shared "migration stimulation factor activity". Moreover, the recitation of a limitation requiring the polypeptide encoded by the members of the claimed genus of nucleic acid molecules to elicit an antibody that binds specifically to "migration

stimulation factor", but not fibronectin, would not reasonably convey to the skilled artisan that, as of the filing date sought, the Applicant had possession of the claimed invention, because the recitation does not provide a description of any uniquely defining or identifying feature that is common to at least a substantial number of members of the claimed genus, which would descriptively set the genus apart from just any polypeptide encoded by a nucleic acid molecule having the required similarity (i.e., at least 90% homology) to the reference amino acid sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

Applicant has further argued that they have interpreted Example 14 of the written description training materials, which are available on the Internet, as suggesting the written description requirement has been met. Contrary to Applicant's remarks, however, the given example does not suggest the written description requirement is satisfied in instances where the claims are directed to polypeptides with 90% *homology* to a disclosed sequence of another polypeptide that possesses a catalytic activity. In fact, as Applicant has later remarked at page 8 of the amendment, the Guidelines state, "[t]he single species disclosed is representative of the genus because all members have **at least 95% structural identity** with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity" (emphasis added). As noted above, the claims in this instance are not directed to nucleic acid molecules encoding polypeptides that are at least 90% identical, but rather polypeptides that are at least 90% homologous to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, provided the polypeptides comprise SEQ ID NO: 41. As also noted above, there is no disclosed, or otherwise known correlation between the presence of the amino acid sequence of SEQ ID NO: 41 in a polypeptide and any ability to stimulate migration of adult skin fibroblasts into a collagen gel. Moreover, the specification altogether fails to characterize any particularly identifying (i.e., substantial) structural feature(s) associated with the ability of a polypeptide encoded by any of the claimed nucleic acid molecules to do so. As a consequence the skilled artisan could not immediately envision, recognize, or distinguish nucleic acid molecules encoding such

polypeptides, and therefore the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Applicant has cited *In re Wallach*, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004). This situation, however, is markedly different from that considered by the Court because the rejected claims in this application are not directed to degenerate nucleic acid molecules encoding a single protein having a disclosed amino acid sequence, but rather to a genus of nucleic acid molecules, which vary structurally and encode polypeptides, which also vary structurally, despite having the common ability to stimulate migration of adult skin fibroblasts into a collagen gel and elicit antibodies that bind a polypeptide comprising SEQ ID NO: 2 but not fibronectin. Moreover, while it is indeed possible for the skilled artisan to envision a genus of degenerate nucleic acid molecules encoding a polypeptide having a known amino acid sequence, the instant specification fails to describe with the requisite particularity the genus of nucleic acid molecules to which the claims are drawn, namely a genus of nucleic acid molecules not limited to degenerate variants encoding a single polypeptide but rather encoding any of a genus of structurally disparate polypeptides described as merely comprising SEQ ID NO: 41. Again, the specification does not describe an association between this particular amino acid sequence and the ability of a polypeptide comprising this amino acid sequence to stimulate migration of adult skin fibroblasts into a collagen gel.

10. The rejection of claims 1, 7-9, 60, and 61 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an isolated, recombinant nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, an isolated, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 from the nucleotide at position 57 through the nucleotide at position 1982, a isolated replicable vector comprising any of said polynucleotide sequences, an isolated host cell comprising said vector, and a method for producing said polypeptide by a process comprising culturing said host cell and isolating said polypeptide, or any nucleic acid molecule taught by the prior art, **does**

not reasonably provide enablement for making and using an isolated nucleic acid molecule having a polynucleotide sequence that is at least 90% homologous to a recombinant polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which comprises the amino acid sequence of SEQ ID NO: 41, stimulates adult skin fibroblasts migration into collagen gel with at least 30% of the same activity of a polypeptide comprising SEQ ID NO: 2 and elicits an antibody that cross-reacts with the polypeptide of SEQ ID NO: 2 without binding fibronectin, a replicable vector comprising said polynucleotide sequence, an isolated host cell comprising said polynucleotide sequence, or a method for producing a polypeptide that stimulates adult skin fibroblasts migration into collagen gel with at least 30% of that activity of a polypeptide comprising SEQ ID NO: 2, said method comprising culturing a host cell comprising said polynucleotide sequence and isolating the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/or the invention commensurate in scope with these claims.

At pages 9 and 10 of the amendment filed April 19, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued, although the claims are directed to nucleic acid molecules encompassing many structures, they are all required to share common structural and functional characteristics. However, as explained above, the specification does not describe an association between this particular amino acid sequence and the ability of a polypeptide comprising this amino acid sequence to stimulate migration of adult skin fibroblasts into a collagen gel. Furthermore, there is no factual evidence of record that reasonably suggests any polypeptide comprising the amino acid sequence of SEQ ID NO: 41 will have at least 30% of the migration stimulation factor activity of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. To the contrary, for the reasons set forth in the preceding Office action, it is apparent that the skilled artisan cannot predict which of such polypeptides might have such activity. In addition, the amount of

guidance and direction set forth in the specification would not be sufficient to enable the skilled artisan to make the claimed nucleic acid molecules that encode polypeptides having such activities because the polypeptide of SEQ ID NO: 2 is not representative of the genus, as a whole, since the amino acids of its sequence, which are essential to its ability to stimulate migration of adult skin fibroblasts into a collagen gel, have not been described; and not only would the skilled artisan not know which amino acids are critical to the function of the polypeptide of SEQ ID NO: 2, but the skilled artisan would not know by which other amino acids those critically important amino acids might be replaced in a variant without loss of that function. This position is supported by the references cited in the preceding Office action.

Applicant has further argued that variants of the polypeptide of SEQ ID NO: 2 can be made, and their ability to satisfy the requirements set forth in the claims can be easily determined. As explained in the paragraph above, while variants of the disclosed polypeptide may be made, it would not be without undue and/or unreasonable experimentation.

In further response to Applicant's argument, Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

Thus, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify nucleic acid molecules encoding polypeptides having the ability to stimulate migration of adult skin fibroblasts into a collagen gel and elicit antibodies that bind a polypeptide comprising SEQ ID NO: 2 but not fibronectin; yet,

defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

In conclusion, careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), reveals a preponderance of factual evidence of record that indicates the disclosure would not be sufficient to have enabled the skilled artisan to make the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Claim Rejections - 35 USC § 103

11. The rejection of claims 1, 7-9, 60, and 61 under 35 U.S.C. 103(a), as being unpatentable over Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, in view of Bendig (of record), is maintained.

At pages 13-15 of the amendment filed April 19, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued the references do not provide assurance that the correct polynucleotide will be obtained. In response, the claims are not directed to any one particular polynucleotide but rather to any nucleic acid molecule encoding a polypeptide having the recited structural and functional features. Given the conventional and routine nature of the methodology used to isolate polynucleotides encoding a polypeptides at the time the invention was made, there is no reason believe such a polynucleotide would not have been obtained.

Applicant has argued the references do not "suggest the recited detail of the polynucleotide encoding MSF (e.g., encoding the polypeptide of SEQ ID NO: 41)". In response, the claims are not directed to a nucleic acid molecule encoding the polypeptide of SEQ ID NO: 41; rather the claims are directed to a genus of structurally

varying nucleic acid molecules having at least 90% homology to a nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which encode polypeptides comprising the amino acid sequence of SEQ ID NO: 41 and have the recited functional characteristics. Encompassed by the claims is a nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2. As explained in the above rejection of claim 9 under 35 U.S.C. 102(b), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, the 70 kDa polypeptide designated "migration stimulation factor (MSF)", which was isolated from cultured fibroblasts by Grey et al., is the polypeptide of SEQ ID NO: 2. Grey et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1). Therefore, as explained in the preceding Office action, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide disclosed by Grey et al. (i.e., the polypeptide of SEQ ID NO: 2) because Grey et al. teaches efforts are underway to do exactly that, and Bendig teaches the methodology necessary to do so was well within the skill of the artisan of ordinary skill at the time the invention was made. Accordingly, as also explained in the preceding Office action, it would have been obvious to one ordinarily skilled in the art at the time of the invention to produce a host cell comprising a vector comprising the cloned polynucleotide sequence encoding the polypeptide by recombinant DNA technology in accordance with the teachings reviewed by Bendig and then culture the host cells and isolate the polypeptide produced by the host cells in the culture. Therefore, among other reasons, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to facilitate production of the polypeptide by recombinant means.

Applicant has argued that the rejection in inappropriate given the holding in the case *In re Bell*, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993) and/or *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995). In reply, MPEP § 2121 states: "[T]he inquiry as to whether a claimed inventions would have been obvious is "highly fact-specific by design". Accordingly, obviousness must be assessed on a case-by-case basis."

Moreover, "reliance on *per se* rules of obviousness is legally incorrect". See *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). Accord *In re Brouwer*, 77 F.3d 422, 426, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996). Therefore, *Bell* should not be regarded as establishing *per se* rules of obviousness.

There is particular reason for not relying upon such decisions as provisions of as *per se* rules, such as: "[I]n view of the rapid advances of science, [...] what may be unpredictable at one time may become predictable at a later time". See *Enzo Biochem. Inc. v. Calgene Inc.*, 188 F.3d 1362, 1374 n. 10, 52 USPQ2d 1129, 1138 n. 10 (Fed. Cir. 1999).

Claims 4 and 5, which are specifically drawn to a nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 or a specific portion thereof, are not rejected as being obvious, since the precise cDNA molecule of claims 4 and 5 would not have been obvious over the Grey et al. teaching of the isolated polypeptide. As Applicant has correctly noted, the redundancy of the genetic code precludes contemplation of or focus on the specific cDNA molecules. What cannot be contemplated or conceived cannot be obvious. See *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

However, to the contrary, a genus of nucleic acid molecules comprising a polynucleotide sequence encoding a polypeptide comprising SEQ ID NO: 2 *can be contemplated and conceived.*

"A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that the DNA molecules encode, while containing a large number of species, is definite in scope and provides the public notice required of patent applicants." *In re Wallach*, 71 USPQ2d 1939, 1942, no. 1 (CA FC 2004).

Indeed, MPEP § 2163 states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely

> known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

This appears precisely the basis of the decision made by the Federal Circuit in deciding *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995) ("The redundancy of the genetic code precluded contemplation of or focus on the **specific** cDNA molecules" [emphasis added]).

Consistently, in the instance, claims 4 and 5, drawn to a nucleic acid comprising a specific polynucleotide sequence encoding the amino acid sequence of the protein, are not rejected as being obvious over the prior art.

As noted above, Grey et al. et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1). There can be no reasonable doubt that at the time the application was filed, one ordinarily skilled in the art would have been motivated to isolate a nucleic acid molecule encoding the isolated protein. Indeed, "the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it". *In re Wallach*, 71 USPQ2d 1939, 1942, no. 1 (CA FC 2004). A rejection upon obviousness, where the prior art "contained detailed enabling methodology for practicing the claimed invention, and evidence suggesting that it would be successful" is appropriate. See *In re O'Farrell*, 853 F.2d 894, 903-904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Furthermore, there is nothing intrinsically wrong in the application of methodology in the rejection of product claims under 35 U.S.C. § 103(a) depending on the particular facts of the case, the manner and context in which methodology applies and the overall logic of the rejection. See *Ex parte Goldgaber*, 41 USPQ2d 1173, 1176 (BPAI 1996) ("We find nothing intrinsically wrong, however, in the application of methodology in rejecting product claims under 35 USC 103, depending on the particular facts of the case, the manner and context in which methodology applies, and the overall logic of the rejection. Nor do we read *Bell* or *Deuel* as issuing a blanket prohibition against the application of methodology in rejecting product claims defining DNA or cDNA.

Furthermore, precedent indicates that it is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound").

Given the state of the art, and the level of skill in the art, the knowledge of the ordinarily skilled artisan, etc., there would have been at least a reasonable expectation of success in isolating a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2. See MPEP § 2143.02. See *O'Farrell*.

Similar decisions have been made by the Board of Patent Appeals and Interferences. See, e.g., *Ex Parte Movva*, 31 USPQ2d 1027 (BPAI 1993).

However, then and now, it appears that the artisan of ordinary skill in the art would not have a reasonable expectation of success in isolating *specific* nucleic acid molecules comprising particular nucleotide sequences, such as the nucleic acid molecules of claims 4 or 5. Thus, while claims 1, 7-9, 60, and 61 are appropriately rejected as being obvious over Grey et al., claims 4 and 5 are not.

Also of relevance, it is noted that it is perfectly acceptable to consider the method by which a compound is made in evaluating the obviousness of the compound. In determining obviousness, it is appropriate to consider such matters as the manner of preparation of the composition vis-a-vis the prior art, the structural similarities as well as differences between the claimed composition and that of the prior art and the presence or absence of properties which would unobvious in view of the prior art. See *In re Pilkington*, 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); *In re Best*, 562, F.2d 1252, 195 USPQ 430 (CCPA 1977).

Furthermore, the Federal Circuit has recognized that a gene, being a chemical compound, could be defined "by its methods of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguished it (from other materials)." See *Amgen*, 927 F.2d 1200 at 1206, 18 USPQ2d at 1021 (Fed. Cir. 1991); *Fiers V. Sugano*, 984 F.2d 1164, 25 USPQ2d 1601 (Fed. Cir. 1993).

Finally, as noted in *In re Cofer*, 354 F.2d 664, 148 USPQ 268 (CCPA 1966), the particular structure or form of a chemical compound is an important consideration in determining obviousness under 35 USC 103; but it is not the only consideration. A compound may well be defined or described by characteristics other than its chemical

structure. Although the artisan may be unaware of the exact chemical structure of a nucleic acid molecule encoding a protein of interest, he or she is aware that is it composed of established relatively unchanging array of nucleotides. Importantly, he or she is also aware that all or part of the amino acid sequence of an isolated protein is readily determined, that a probe can be designed using the information acquired, which will hybridize with a nucleic acid molecule encoding the protein, and that established methodology, which was both routine and conventional at the time of the invention, is used to isolate the nucleic acid molecule encoding the protein by virtue of the selective hybridization of the probe to this nucleic acid molecule. Such technical procedures are taught in the prior art references of record, which have been employed by Applicant in the instant disclosure to enable the skilled artisan to make and use the claimed invention.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

12. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Claim 1 recites, "a polynucleotide with at least 90% homology thereto encoding a polypeptide comprising the amino acid sequence of VSIPPRNLGY (SEQ ID NO: 41), wherein the polynucleotide has the following characteristics: (a) the polypeptide it encodes has at least 30% of the migration stimulation factor activity of a polypeptide having the amino acid sequence of SEQ ID NO:2 [...]; and (b) the polypeptide it encodes elicits antibodies that recognize a polypeptide having the amino acid sequence of SEQ ID NO: 2, but. do not recognize fibronectin".

At page 6 of the amendment filed April 19, 2006, Applicant has asserted that support for the amendment to the claims is found throughout the specification.

However, it appears that Applicant has not pointed to any particular disclosure in the specification, including the claims, as originally filed, which is believed to provide the necessary support.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims". See MPEP § 714.02 and § 2163.06. Nevertheless, as MPEP § 2163 further states: "The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See Wertheim, 541 F.2d at 263, 191 USPQ at 97".

Although the specification, as originally filed, describes two polypeptides (i.e., the polypeptide of SEQ ID NO: 2, and the immunogenic, synthetic peptide of SEQ ID NO: 5), which comprise the amino acid sequence of SEQ ID NO: 41, the specification has not described with any degree of particularity a genus of nucleic acid molecules encoding a genus of polypeptides comprising this amino acid sequence, which have at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel and which have the ability to elicit antibodies that bind a polypeptide comprising SEQ ID NO: 2 but not fibronectin. Furthermore, while at page 46 of the substitute specification filed June 8, 2005, there is a description of monoclonal antibodies, which are raised using immunogens that are synthetic peptides based on the 10 amino acid unique tail of MSF (i.e., the amino acid sequence of SEQ ID NO: 41), or on any of the peptide sequences of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9, this description does not suffice to provide proper and sufficient support for the language of the claims because it does not describe a genus of polypeptides comprising the amino acid sequence of SEQ ID NO: 41, which have at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel and which have the ability to elicit antibodies that bind a polypeptide comprising SEQ ID NO: 2 but not fibronectin.

This issue might be resolved if Applicant were to point to particular disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary support for the language of the present claims.

Claim Rejections - 35 USC § 102

13. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/31233 A1.

WO 99/31233 A1 (Schor et al.) teaches a polynucleotide encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2, which comprises the amino acid sequence of SEQ ID NO: 41; see entire document (e.g., claim 18). Furthermore, Schor et al. teaches the polypeptide has migration stimulating factor activity and elicits antibodies that bind to the polypeptide but not to fibronectin; see, e.g., claims 6 and 27. In addition, Schor et al. teaches an isolated replicable vector comprising a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2; see, e.g., claim 7. Schor et al. teaches an isolated host cell comprising a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2; see, e.g., claim 8. Schor et al. teaches making a polypeptide comprising an amino acid sequence identical to SEQ ID NO: 2 by a process that comprises transfecting a host cell with a polynucleotide encoding the polypeptide, or a vector comprising such a polynucleotide, and isolating the polypeptide; see, e.g., claim 9.

Because the amino acid sequence of the disclosed polypeptide is identical to SEQ ID NO: 2, the disclosed polypeptide is expected to have 100% of the migration stimulation factor activity of a polypeptide having such an amino acid sequence, wherein said activity refers to the ability to stimulate adult skin fibroblast migration into a collagen gel.

Conclusion

14. Claims 4, 5, and 29 are allowed; no other claim is allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
June 20, 2006